CASE 4-100-8303C/C1D1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF

SCHULER ET AL.

APPLICATION NO:

FILED:

FOR: USE OF RAPAMYCIN DERIVATIVES IN VASCULOPATHIES AND XENOTRANSPLANTATION

Assistant Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Sir:

Prior to the examination of the above-referenced patent application, please amend the application as follows:

In the Specification:

Please insert the following as the first paragraph beneath the title on page 1:

-- This application is a divisional of US Patent Application No. 09/712,359, filed November 14, 2000, which is a continuation of 09/155,210, filed September 23, 1998, abandoned, which is a 371 of PCT/EP97/01548, filed March 26, 1997 which are herein incorporated by reference. --.

In the Claims:

Cancel claims 1-10 and replace them with new claims 11-28.

-- 11. (new) A method for preventing or treating:

neointimal proliferation and thickening and/or restenosis and/or vascular occlusion following vascular injury, or

manifestations of chronic rejection in a recipient of organ or tissue transplant, or

acute or chronic rejection in a recipient of organ or tissue xenograft transplant,
comprising administering to the patient an effective amount of 40-O-(2-hydroxy)ethyl-rapamycin with an effective amount of a second agent selected from the group consisting of a cyclosporin or an immunosuppressive analog thereof, an ascomycin or immunosuppressive analog thereof, a corticosteroid, cyclophosphamide, azathioprene, methotrexate, brequinar, leflunomide, mizoribine, mycophenolic acid, mycophenolate mofetil, 15-deoxysperguatine, immunosuppressive monoclonal antibodies, and CTLA4-Ig.

12. (new) The method of Claim 11 wherein the second agent is cyclosporin A, cyclosporin G, FK-506 or monoclonal antibodies to leukocyte receptors or to their ligands.

13. (new) The method of Claim 11 wherein the second agent is monoclonal antibodies to MHC, CD2, CD3, CD4, CD7, CD25, CD28, B7, CD45, CD58, or to ligands thereof.

14. (new) The method of Claim 13 wherein the second agent is monoclonal antibodies to CD3.

15. (new) The method of Claim 11 wherein the second agent is cyclosporin A.

16. (new) The method of Claim 11 wherein the second agent is cyclosporin G.

17. (new) The method of Claim 11 wherein the second agent is mycophenolic acid.

18. (new) The method of Claim 11wherein the second agent is CTLA4Ig.

19. (new) The method of Claim 11 wherein the second agent is mycophenolate mofetil.

20. (new) A method for preventing or treating:
neointimal proliferation and thickening and/or restenosis and/or vascular occlusion following vascular injury,
comprising administering to the patient an effective amount of 40-O-(2-hydroxy)ethyl-rapamycin with an effective amount of a second agent selected from the group consisting of a cyclosporin or an immunosuppressive analog thereof, an ascomycin or immunosuppressive analog thereof, a corticosteroid, cyclophosphamide, azathioprene, methotrexate, brequinar, leflunomide, mizoribine, mycophenolic acid, mycophenolate mofetil, 15-deoxysperguatine, immunosuppressive monoclonal antibodies, and CTLA4-Ig.

21. (new) The method of Claim 20 wherein the second agent is cyclosporin A, cyclosporin G, FK-506 or monoclonal antibodies to leukocyte receptors or to their ligands.

22. (new) The method of Claim 20 wherein the second agent is monoclonal antibodies to MHC, CD2, CD3, CD4, CD7, CD25, CD28, B7, CD45, CD58, or to ligands thereof.

23. (new) The method of Claim 22 wherein the second agent is monoclonal antibodies to CD3.

24. (new) The method of Claim 20 wherein the second agent is cyclosporin A.

25. (new) The method of Claim 20 wherein the second agent is cyclosporin G.

26. (new) The method of Claim 20 wherein the second agent is mycophenolic acid.

27. (new) The method of Claim 20 wherein the second agent is CTLA4Ig.

28. (new) The method of Claim 20 wherein the second agent is mycophenolate mofetil. --

REMARKS

Favorable consideration of this application is respectfully requested.

Respectfully submitted,

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